REMARKS

Claims 61-63, 65-68, 77, 79-81, 86, 87, 91, 93-101 and 104-115 were pending. Claims 96-100 were previously withdrawn. Claims 67 and 68 have been canceled in the present amendment, and claim 96 has been amended to correct a dependency upon a previously canceled claim. Thus, upon entry of this amendment, claims 61-63, 65-66, 77, 79-81, 86, 87, 91, 93-101 and 104-115 will be pending in the application.

No new matter has been added.

Applicants reserve the right to pursue the subject matter of the claims as originally filed in this application or in another related application. In view of the foregoing claim amendments and the arguments set forth below, Applicants respectfully submit that the claims are now in condition for allowance.

Acknowledgement of Withdrawal of Previous Rejections

Applicants gratefully acknowledge the withdrawal of the following previous rejections:

The Examiner has withdrawn the rejection of claim 61 under 35 U.S.C. §112, second paragraph as being rendered vague and indefinite by the use of the phrase "binding affinity of about."

The Examiner has withdrawn the rejection of claim 86 under 35 U.S.C. §112, second paragraph as being rendered vague and indefinite by being dependent on a canceled claim.

The Examiner has withdrawn the rejection of claims 61-63, 65-68, 77, 79-81, 86-87, 91, 93-95, 101, and 104-115 under 35 U.S.C. §112, first paragraph, based on the limitation "binding affinity of about 10^{-8}M."

The Examiner has withdrawn the rejection of claims 61-62, 65-67, 81, 86-87, and 93 under 35 U.S.C. §102(b) as being anticipated by Hamada *et al.* 1984, Microbiol. Immunol. Vol. 28 No. 9 pgs. 1009-1021 in light of Roitt *et al*, 1993, Immunology, 3rd Edition, Mosby, St.

The Examiner has withdrawn the rejection of claims 107-109, and 111-115 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

Objections of Claim 67

The Examiner has objected to claim 67 because the limitation of "Gram positive bacteria is fixed to a solid support" does not further limit the structure of the claimed antibody. Solely in

order to expedite prosecution, Applications have canceled claims 67 and 68. Accordingly, this objection is rendered moot.

Rejection of Claims 61, 77, 79-81, 86-87, 93, 95, 101 and 104-115

Under Doctrine of Obviousness-type Double Patenting

The Examiner has maintained the rejection of claims 61, 77, 79, 93 and 95 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-7, 9-12 and 14-19 of U.S. Patent No. 6,610,293. The Examiner has also maintained the rejection of claims 61, 101 and 104-115 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-6, 9-12 and 14-19 of U.S. Patent No. 6,610,293. Applicants will consider filing a terminal disclaimer over the 6,610,293 patent when the remaining rejections have been overcome.

The Examiner has maintained the provisional rejection of claims 77, 81, 86-87 and 93 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-58 and 79-83 of copending Application No. 11/193,440. The Examiner has also maintained the provisional rejection of claims 104-115 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53, 83, 91-92 and 96 of copending Application No. 11/193,440. If appropriate, Applicants will address any obviousness-type double patenting issues upon an indication of allowance of claims in Application No. 11/193,440 or in the instant application. Applicants will consider filing a terminal disclaimer over the patent due to issue from Application No. 11/193440 when the remaining rejections have been overcome.

The Examiner has also maintained the provisional rejection of claims 77, 79-81, 86-87 and 93 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-43, 47-68 and 72 of copending Application No. 10/323,926. This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. If appropriate, Applicants will address any obviousness-type double patenting issues upon an indication of allowance of claims in Application No. 10/323,926 or in the instant application.

Rejection of Claims 61-63, 65-68, 79-81, 86, 87, 91, 94, 101 and 114-115
Under Section 112, First Paragraph

The Examiner has rejected claims 61-63, 65-68, 79-81, 86, 87, 91, 94, 101 and 114-115 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description

requirement. In particular, the Examiner asserts that the specification has not adequately described the antigenic determinants (immunoepitopes) and "fails to adequately describe at least a substantial number of members of the genus of the monoclonal antibody aforementioned above to which the claims are based."

Applicants respectfully traverse the foregoing rejection. The claims are in compliance with the written description requirement of 35 U.S.C. §112, first paragraph as the specification clearly conveys possession of the claimed invention to one of skill in the art. As the presently claimed invention relates to monoclonal antibodies which specifically bind to a fully characterized antigen, *i.e.,* poly-glycerol phosphate of LTA of Gram positive bacteria, the written description requirement is met.

The present claims are directed to a composition comprising an amount of an isolated monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier, wherein the antibody ***specifically binds to poly-glycerol phosphate of Lipoteichoic acid*** (LTA) of Gram positive bacteria and is of the IgG isotype. The claimed antibodies also bind to and enhance opsonization of multiple serotypes of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans* by phagocytic cells with or without complement as compared to an appropriate control in an *in vitro* opsonization assay.

To comply with the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventors had possession of the claimed invention. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). The present specification provides adequate written description of the claimed genus of monoclonal antibodies directed to a fully characterized antigen, poly-glycerol phosphate of LTA of Gram positive bacteria.

Regarding antibody claims, the Court of Appeals for the Federal Circuit has held that "as long as an applicant has disclosed a 'fully characterized antigen,' either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004). The court, when considering an antibody defined by function rather than structure, has looked to the USPTO Written Description

Guidelines as persuasive authority, stating that "a claim directed to 'any antibody which is capable of binding to antigen X' would have sufficient support in a written description that disclosed 'fully characterized antigens.'" *Noelle*, 355 F.3d 1343, 1349. Example 14 of the revised Written Description Training Materials (Revision 1, March 23, 2008), clearly states that "an adequate description of a purified antigen would have put an inventor in possession of antibodies which bind to the purified antigen." This precedent was followed by the Board of Patent Appeals and Interferences in a recent decision in which a claim to monoclonal antibody that "binds an epitope within amino acids 412-562 of the progesterone receptor B form" was found to be supported by an adequate written description. *Ex parte* Hiaying Xia and Zhida Huang. Appeal 2008-3329 (Application 10/242,092). Decided January 28, 2009. The Board reasoned as follows:

> The Examiner appears to be requiring that the Specification disclose both the specific epitope recognized by the antibody (*see, e.g.*, FF10), as well as the structure of the antibody (*see, e.g.*, FF9). ***All that is required, however, for adequate written description of an antibody is the disclosure of a fully characterized antigen***, which requirement is met by the Specification (FF5). ***We decline to read into that requirement that the Specification also disclose the specific epitope bound by the antibody, or the structure of the antibody.*** (***emphasis added***)

The presently claimed monoclonal antibodies ***specifically bind poly-glycerol phosphate of LTA of Gram positive bacteria***. Poly-glycerol phosphate is a fully characterized antigen. Its chemical structure is described in the present specification and was well known in the art at the time of filing (*e.g.*, see Fisher *et al.* On the basic structure of poly(glycerolphosphate) lipoteichoic acids. *Biochem. Cell Biol.* vol. 68, 1990, submitted herewith as Appendix A). Moreover, because the LTA backbone is composed of repeating units of poly-glycerol phosphate, it represents a small number of defined and well characterized epitopes Because the present claims are directed to antibodies that bind a fully characterized antigen, namely poly-glycerol phosphate of LTA of Gram positive bacteria, the written description requirement has been met. Despite this legal precedent, the Examiner, however, asserts that "absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of a composition comprising a monoclonal antibody with the recited activities." As stated by the Board in *Ex Parte Xia*, the specific epitope

recognized by the antibody need not be disclosed. This is despite the fact that there is significant epitope variability in an amino acid protein of 151 amino acid residues recited in the claims before the Board in *Ex Parte Xia*. As the only element needed for an antibody to meet the written description requirement is the disclosure of a fully characterized antigen, the Examiner's reliance on Greenspan *et al.* (Nature Biotech. 7:936-937, 1999) with respect epitope variability is not relevant. As the present specification discloses a fully characterized antigen, LTA of Gram positive bacteria, the present claims satisfy the written description requirement.

Furthermore, with respect to generic claims, the Court has held that it is not necessary that every permutation within a generally operable invention be effective for an applicant to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). Likewise, it is well established that for claims directed to genetic material, "a statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." *Regents of the University of California v. Eli Lilly and Co.,* 119 F. 3d, 1559, 1568, 43 USPQ2d 1398 (Fed. Cir. 1997). Applicants note that the facts in *Eli Lilly* are not analogous with to the present application. The claims of the present application, however, recite more than a mere function. In particular, claim 61 provides a recitation of structural features common to members of the genus of monoclonal antibodies in that the members of the genus have the common structural feature of being specifically binding a fully characterized antigen, poly-glycerol phosphate of LTA of Gram positive bacteria and are of the IgG isotype. In addition, the specification teaches that there is a correlation between the structure of a monoclonal antibody which specifically binds poly-glycerol phosphate of LTA and the function of binding to and enhancing opsonization of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans* (*see e.g.,* Examples 2, 3 and 7). Moreover, Applicants have described at least 3 antibodies of the claimed genus.

In particular, Example 1 of the present specification describes the preparation of monoclonal antibodies (and hybridomas) made using an antigen preparation from heat killed *S. epidermidis*. Examples 2 and 3 further show that the resultant antibodies are opsonic, and that they confer *in vivo* protective effects against *staphylococci*. Example 7 of the specification further shows binding of an antibody within the scope of the present claims (Ab 96-110, also

referred to as "A110") to LTA from *S. mutans*, *S. aureus* and *S. faecalis* (Tables 8 and 9 of the specification) and that it enhances the opsonization for both coagulase positive and coagulase negative staphylococci (see page 53, paragraph 2 of the specification). A chimeric version of this antibody was also created and shown to be opsonic and provide protective efficacy *in vivo* (see Examples 11-13 of the specification).

This disclosure provides a person of ordinary skill in the art with structural information for every member of the genus (*i.e.,* the ability to specifically bind a fully characterized antigen, poly-glycerol phosphate of LTA) that falls within the scope of the claim as well as a correlation with the functional characteristics possessed by members of the genus and recited in the claims. In view of this disclosure, one skilled in the art would reasonably conclude that the inventors had possession of a composition of monoclonal antibodies which specifically bind LTA of Gram positive bacteria and enhance opsonization of multiple serotypes of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans*.

That Applicants provide a disclosure sufficient to demonstrate possession of the claimed genus of monoclonal antibodies is further demonstrated by the identification and characterization of additional anti-LTA antibodies within the scope of the present claims (*see, e.g.,* U.S. Pub. No. 2004/0052779). Two monoclonal antibodies, A120 and 391.4, having a high degree of sequence similarity to the A110 antibody (which corresponds to the same CDR regions as Ab 96-110 of the present application[1]), were identified by Applicants and shown to specifically bind LTA and bind to and enhance opsonization of Gram positive and negative bacteria.[2] In fact, the Applicants observed "the level of homology between the M110, M120, and MAb-391.4 variable regions may indicate that opsonic antibodies to LTA recognize a nearly identical epitope using nearly identical modes of binding, and that this mode of binding is important to their functional activity."[3]

In view of the above, the present specification describes the claimed invention in sufficient detail that one of ordinary skill in the art can reasonably conclude that the inventors were in possession of the claimed invention at the time of filing. Applicants, therefore, request reconsideration and withdrawal of this rejection.

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[1] Antibodies A110 and 96-110 differ only in the terminal amino acids of the light chain (*i.e.,* one amino acid difference on each of the N and C terminal positions).
[2] See Examples 1, 2, 5, 6, and 8 of the '779 Publication and Examples 2, 7, and 11 of the present Application.
[3] See paragraph [0196] of the '779 Publication.

Rejection of Claims 77, 79-81, 86-87,91, 93-95, and 104-113 Under Section 112, First Paragraph

The Examiner has rejected claims 77, 79-81,86-87,91, 93-95, and 104-113 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner states:

> Applicant has not demonstrated that a composition comprising variants of monoclonal antibody of IgG isotype aforementioned above is capable binding to polyglycerol phosphate of LTA of all gram positive bacteria species discussed above....
> ...Moreover, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Also the specification fails to disclose which variable regions of the heavy and light chain of a monoclonal antibody of SEQ ID NO: 87 and 89; and of the monoclonal antibody 96-110 that are essential to the function of the immunoepitope and are able to retains its the activity.[4]

Applicants respectfully traverse this rejection. As noted above, and contrary to the Examiner's suggestion, claims directed to a genus of monoclonal antibodies are adequately described based on the disclosure of a fully characterized antigen. Polyglycerol phosphate of LTA is a fully characterized antigen. Accordingly, claims 77, 79-81,86-87,91, 93-95, and 104-113 meet the written description requirement. Furthermore, the rejected claims are supported by a structure function correlation which requires the claimed antibodies, or antigen binding fragments thereof, to specifically bind to poly-glycerol phosphate of LTA of Gram positive bacteria.

Moreover, Applicants note that claims 77, 93, 95, 104, and 105 are directed to specific antibodies comprising the antigen binding regions (CDRs) set forth in SEQ ID NO: 87 or SEQ ID NO:89 (claim 77), antibodies having the specific heavy or light chain variable regions set forth in SEQ ID NO:s 87 and 89 (claims 104 and 105), or antibodies having 70% identity or more to the heavy or light chain variable genes set forth in SEQ

[4] Pages 11-12 of the instant Office Action

ID NO: 87 or 89. Claims dependant upon claim 77 further require that the claimed antibodies, or antigen binding fragments thereof, specifically bind to poly-glycerol phosphate of LTA of Gram positive bacteria.

Example 5 of the Written Description Training Materials specifically outlines a situation where a genus of claimed proteins are defined by their function (*i.e.,* ability to bind a second protein) and a partial protein sequence (*i.e.*, SEQ ID NO:1 having only 10 amino acids). In such a fact pattern, the Training Materials note that a claim meets the written description requirement. Likewise, the recitation of a particular amino acid sequence (*e.g.,* SEQ ID NO: 87 or SEQ ID NO:89) coupled to the specific functional requirement of binding to a poly-glycerol phosphate provides a correlation between structure and function of the antibodies and therefore meets the written description requirement.[5]

In summary, because the claimed antibodies, or antigen binding fragments thereof are directed to a fully characterized antigen, and, alternatively, because the claimed antibodies are described to have a clear correlation between their structure and function, Applicants request the rejection of claims 77, 79-81,86-87,91, 93-95, and 104-113 under 35 U.S.C. § 112, first paragraph be withdrawn.

[5] Also see In re Alonso, 2008 U.S. App. LEXIS 24320, 16-17 (Fed. Cir. Oct. 30, 2008) stating: "...we have found adequate written descriptive support for a claimed invention where the disclosure specifies ..... functional characteristics when coupled with a known or disclosed correlation between function and structure....' Enzo, 323 F.3d at 964"

Rejection of Claims 61-63, 65-68, 79-81, 86-87, 91, 94, 101, and 114-115 Under Section 112, First Paragraph

The Examiner has rejected claims 61-63, 65-68, 79-81, 86-87, 91, 94, 101, and 114-115 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In particular, the Examiner alleges that the "specification is not enabled for a composition comprising an amount of an isolated a monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier." The Examiner further alleges that the specification does not enable a person skilled in the art to make and use the claimed invention.

Applicants traverse the foregoing rejection on the grounds that the amount of direction and guidance disclosed in the specification is sufficient to enable the skilled artisan to make and use the claimed invention.

The Examiner acknowledges that the specification discloses an antibody that promotes clearance of staphylococci from the blood and promotes survival of mice upon treatment with an antibody of the invention. However, the Examiner insists that the specification is limited to survival of neonates and cannot be drawn to *prevention* of staphylococcus infection. This is based upon the Examiner's construction of the term "prevention" to be equivalent to administration of a vaccine. Applicants note that the present claims are not directed to a vaccine or an active immunization in which an antigen or fragment thereof is administered to a host to induce a protective immune response to antigen. Instead, the present invention is directed to a composition comprising anti-LTA monoclonal antibodies which have been shown to opsonize multiple Gram positive bacteria and to protect against infection when administered in vivo. Thus, there is no need for the host to generate a protective antibody response to invading bacteria, as the monoclonal antibody compositions of the invention provide protection against staphylococcal infection. The specification describes protective administration of a composition of the present invention on page 23:

> A further embodiment of the present invention is a method of preventing such infections, comprising administering a prophylactically effective amount of a pharmaceutical composition comprising the anti-LTA antibody (whether polyclonal or monoclonal or chimeric, including fragments, regions, and derivatives thereof) and a pharmaceutically acceptable carrier.

> A prophylactically effective amount is an amount reasonably believed to provide some measure of prevention of infection by Gram positive bacteria.

Accordingly, prevention, as presently claimed, is not equivalent to vaccination, but involves treatment or prophylactic treatment of a subject.

Furthermore, the present specification fully enables one of skill in the art to make and use the claimed invention because the specification discloses methods to make and test antibodies of the invention, and because the specification demonstrates their use. According to the MPEP:

> "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." MPEP 2164.01(b)
>
> and
>
> "If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied." MPEP 2164.01(c)

As described above, the specification describes prophylactic and preventative treatment using antibodies of the invention. Assays to determine clearance of bacteria and protection are described in the specification at least on page 32, paragraph 2 through page 33. Example 2 describes the ability of an antibody of the invention to opsonise bacteria and states that "[s]uch an antibody would be capable of promoting clearance of Staphylococci that have invaded a host and would be useful therapeutic agent." Furthermore, Example 3 (entitled "In Vivo Protective Efficacy) demonstrates that administration of an antibody of the invention before and after infection confers enhanced survival, thereby demonstrating that the antibody confers a protective effect.

The Examiner provides a discussion of several of the Wands factors (MPEP 2164.01(A)), and we address the Examiner's points individually as follows.

Nature of the Invention

The Examiner asserts that the claims as drawn to any composition comprising an isolated monoclonal antibody of IgG isotype effective to prevent staphylococcal infection

in neonates. In contrast to the Examiner's characterization, the present claims are directed specifically to anti-LTA antibodies, not ***any*** antibody isotype effective to prevent staphylococcal infection in neonates.

Breadth of the claims

As the Examiner describes, the claims encompass any composition comprising an isolated monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier, wherein the antibody specifically binds to poly-glycerol phosphate of Lipoteichoic acid (LTA) of Gram positive bacteria and is of the IgG isotype, wherein the antibody binds to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans* by phagocytic cells. However, techniques for making antibodies are routine in the art, and require no undue experimentation. Moreover, the specification provides ample guidance for producing the presently claimed antibodies. In particular, Example 1 describes preparation of an antigen and production of candidate immunoglobulin molecules. Examples 2 and 3 describe methods to test the opsonic effect of antibodies, and demonstrate that administration of an antibody of the invention before and after infection confers enhanced survival, thereby demonstrating that the antibody confers a protective effect. Example 7 of the specification describes methods to test whether an exemplary antibody of the invention binds the LTA of staphylococci. Examples 11-13 further describe methods to humanize antibodies of the invention.

Moreover, the level of one of ordinary skill is high. A skilled artisan would clearly understand, given the state of the art at the time of filing and the disclosure of the present specification, how to make and use antibodies of the present invention.

Guidance of the Specification/ Existence of Working Examples

As described above, the guidance provided by the Specification is extensive. The Specification provides 13 Examples describing antigen preparation, antibody and hybridoma creation (Example 1), tests for opsonic activity (Examples 2 and 11),

description and testing of in vivo protection (Examples 3 and 12), binding and antigen characterization (Examples 4-7), humanization (Example 8), and chimeric antibody production (Examples 9 and 10).

The Examiner insists that "[t]he claimed invention is drawn to prevention of staphylococcal infection and as a result prevention is correlated to a vaccine. A vaccine by definition must provide protection against an infection demonstrable by challenge experiments." However, as explained above, the present invention is not directed to active immunization, but rather to the administration of protective antibodies to the host.

The Examiner asserts that the data "merely" shows that the composition increases the number of neonates that survive a Staphylococcal infection and thus fails to show prevention or protection against Staphylococcus species. Applicants submit that the evidence of increased survival shown in Examples 3 and 12 is affirmative evidence of protection and therefore prevention of Staphylococcal infection. The claimed antibodies are clearly shown to be successful in treating and protecting animals from Staphylococcal infection.

State of the Art

The Examiner discusses active immunization in general and cites several sources in the "vaccine art" that describe the ability of an antigen to stimulate an immune response in a host. The Examiner's discussion and the cited references are not relevant because the present invention is not drawn to methods of active immunization, but, as described above, to administration of a composition of anti-LTA antibodies to neonates to prevent Staphylococcal infection.

The use of antibodies as a prophylactic agent to prevent or reduce the effects of an infection is well established in the art. Indeed, antibody compositions have been successfully used to treat or prevent infection by a wide variety of pathogenic agents including viruses, bacteria, and toxins. For example, Volk *et al.*[6] showed that administration of monoclonal antibodies is effective to neutralize tetanus toxin. In their studies, toxin was mixed with monoclonal antibodies and, after a short incubation,

[6] Infection and Immunity. 1984. 45(3):604-609. Enclosed herewith as Appendix A.

injected into mice. Mice still surviving on day 4 (where control mice died on days 2 or 3) were considered protected from the toxin. Indeed, antibody compositions directed to tetanus toxin are currently being used in the clinic to protect patients who are potentially exposed to tetanus. HyperTet™ S/D is one example of an immunogloblulin composition which may be administered to patients to neutralize tetanus toxin.[7]

Likewise, monoclonal antibodies have been used to prevent viral and bacterial infection. For example, Meuleman *et al.*[8] showed that prophylactic administration of anti-CD81 antibodies was effective at preventing Hepatitis C virus infection in animals[9]. Similarly, Rosok *et al.*[10] found that administration of monoclonal antibodies against the flagellum of *Pseudomonas aeruginosa* "provided specific and significant prophylactic and therapeutic protection."[11] Rosok *et al.* found that all animals which received antibody injections prior to bacterial infection survived, as compared to about 20% survival in control animals.[12] Rosok *et al.* also showed that the monoclonal antibodies were effective for treating animals after infection, where 70%-90% of treated post-infection animals were protected.[13]

Similar to the composition of Rosok *et al.*, the presently claimed invention is directed to a composition of monoclonal antibodies against pathogenic bacteria. As described in Applicants' specification, administration of a composition of anti-LTA antibodies protected animals from infection. Specifically, in Example 3 of the present specification Applicants showed that administration of an antibody composition of the invention prior to and after bacterial infection enhanced survival in a rat neonate model. Example 12 of the specification further shows protective efficacy of a chimeric antibody of the invention for Adult CF1 mice against bacterial infection, while Example 13 shows efficacy of the chimeric antibody in a neonatal rat model. Accordingly, Applicants specification demonstrates the efficacy of administering a composition of anti-LTA antibodies to treat or prevent Staphylococcal infection.

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[7] See the information provided online by Talecris Biotherapeutics: http://www.talecris-pi.info/inserts/hypertet.pdf .
[8] Hepatology. 2008. 48(6):1761-1768. Enclosed herewith as Appendix B.
[9] Meuleman *et al.* at page 1764, column 1
[10] Infection and Immunity. 1990. 3891-3821. Enclosed herewith as Appendix C.
[11] See Rosok *et al.* Abstract, page 3819
[12] Rosok *et al.* at page 3824, column 2.
[13] Rosok *et al.*, at page 3825, column 1.

Finally, there are FDA approved antibody compositions currently in use in humans to treat and prevent pathogenic infection. For example, the drug Synagis® (Palivizumab) is a protective antibody against respiratory syncytial virus (RSV). The manufacturer, MedImmune, describes Synagis® as follows: "Even though Synagis is given as a shot by your healthcare provider, ***it's not a vaccine and it works differently. Each Synagis shot provides a dose of virus-fighting substances called antibodies that help prevent RSV from infecting your baby's lungs***"(***emphasis added***).[14] Thus, like the presently claimed composition, Synagis® is administered to high-risk infants ***prior to RSV infection to prevent disease***, although regular administration may be continued after infection.

Moreover, since the time of filing, antibodies of the present invention have been tested in clinical trials and found to be safe in both adults and neonates. One particular antibody, Pagibaximab®, has been shown to be effective against >90% of coagulase negative staphylococci strains, and demonstrate >90% bacterial killing at <10μg/ml.[15]

In summary, a skilled artisan would understand, given the disclosure of the specification, how to make and use the presently claimed invention. Furthermore, the amount of guidance provided by the specification (as evidenced above) and the successful application of art-recognized antibodies for prophylaxis and treatment of disease would have led the skilled artisan to expect that the present invention would be useful as claimed with no undue experimentation. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 61-63, 65-68, 79-81, 86-87, 91, 94, 101, and 114-115 under 35 U.S.C. § 112, first paragraph.

[14] Taken from "http://www.synagis.com/how-synagis-works.aspx" on July 8, 2009.
[15] See page S32, column 2 of Weisman. Archives de pediatrie 14 (2007) S31-S34, enclosed herewith as Appendix D.

CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400. If there are any fees due, please charge our Deposit Account No. 12-0080, under Order No. SYNI-003CN from which the undersigned is authorized to draw.

Dated: July 17, 2008

Respectfully submitted,

Electronic Signature: /Amy E. Mandragouras/
Amy E. Mandragouras, Esq.
Registration No.: 36,207
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicants